

What is claimed is:

1. (Previously presented) A method of identifying a marker useful for detecting diabetes, said method comprising:
 - a) using an oligonucleotide of predetermined sequence, detecting a presence in RNA of blood samples which have not been fractionated into cell types from subjects having diabetes, of RNA encoded by a gene, said gene expressed in blood and in a non-blood tissue of a subject not having diabetes, said oligonucleotide being specific only for RNA, or cDNA complementary to said RNA, encoded by said gene in said samples,
 - b) quantifying a level of said RNA encoded by said gene; and
 - c) determining a difference between said quantified level and a quantified level of a control RNA encoded by said gene in RNA of blood samples which have not been fractionated into cell types from control subjects, said control RNA having been detected in said samples from said control subjects, thereby identifying said gene as being a marker useful for detecting diabetes.
2. (Previously presented) A method of identifying two or more markers useful for detecting diabetes, said method comprising:

for each of a collection of two or more genes;

 - a) using an oligonucleotide of predetermined sequence, detecting a presence in RNA of blood samples which have not been fractionated into cell types from subjects having diabetes, of RNA encoded by said gene, said oligonucleotide being specific only for RNA, or cDNA complementary to said RNA, encoded by said gene in said samples, said gene being expressed in blood and in a non-blood tissue of a subject not having diabetes;
 - b) quantifying a level of said RNA encoded by said gene; and
 - c) determining a difference between said quantified level and a quantified level of control RNA encoded by said gene in RNA of blood samples which have not been fractionated into cell types from control subjects, said control RNA having been detected in said samples from said control subjects,

thereby identifying said two or more genes as two or more markers useful in detecting

diabetes.

3. (Previously presented) A method of identifying a marker useful for detecting diabetes, said method comprising:

- a) producing amplification products from RNA of blood samples which have not been fractionated into cell types, from subjects having diabetes, using primers specific only for RNA, and/or cDNA complementary to said RNA, encoded by a gene in said samples, said gene being expressed in blood and in a non-blood tissue of a subject not having diabetes;
- b) quantifying a level of said amplification products; and
- c) determining a difference between said quantified level of said amplification products and a quantified level of amplification products produced using primers specific only for RNA, and/or cDNA complementary to said RNA, encoded by said gene from control RNA, in RNA of blood samples which have not been fractionated into cell types, said control RNA having been detected in said samples from said control subjects,

thereby identifying said gene as being a marker useful for detecting diabetes.

4. (Previously presented) A method of identifying two or more useful for detecting diabetes, said method comprising :

for each of a collection of two or more genes;

- a) producing amplification products from RNA of blood samples which have not been fractionated into cell types from subjects having diabetes, using primers specific only for RNA, and/or cDNA complementary to said RNA, encoded by said gene of said subjects, wherein said gene is expressed in blood and in a non-blood tissue of a subject not having diabetes;
- b) quantifying a level of said amplification products; and
- c) Determining a difference between said quantified level of said amplification products and a quantified level of amplification products produced using primers specific only for RNA, and/or cDNA complementary to said RNA, encoded by said gene, from control RNA in RNA of blood samples which have not been

fractionated into cell types, from control subjects, said control RNA having been detected in said samples from said control subjects,
thereby identifying said collection of said two or more genes as two or more markers useful for detecting diabetes.

5. (Previously presented) The method of any one of claims 1-4, wherein each of said one or more markers corresponds to a non immune response genes.

6. (Canceled)

7. (Previously presented) The method of any one of claims 1-4, wherein each of said one or more markers corresponds to a gene expressed by non-lymphoid tissue.

8.(Original) The method of any one of claims 1-4, wherein said diabetes is either symptomatic or asymptomatic.

9. (Previously presented) The method of any one of claims 1-4, wherein said diabetes is type II diabetes.

10.(Original) The method of any one of claims 1-4, wherein said one or more markers identifies one or more genes selected from the group of genes listed in Table 3G.

11. (Canceled)

12. (Previously presented) A method of detecting a difference in expression of a gene in a human test subject as compared with human control subjects, said method comprising:

- a) using an oligonucleotide of predetermined sequence, detecting in RNA of a blood sample from said test subject which has not been fractionated into cell types, RNA encoded by said gene in said sample, wherein said gene is expressed in blood and in a non-blood tissue in a subject who is not said test subject, said oligonucleotide being specific only for RNA or cDNA complementary to said RNA, encoded by said gene;
- b) quantifying a level of said RNA encoded by said gene; and
- c)determining a difference between said level and a quantified level of control RNA encoded by said gene in RNA of blood samples which have not been fractionated into cell types from said control subjects, wherein said difference is

indicative of diabetes in said test subject,
thereby detecting a difference in expression of said gene in said human test subject vs. said human control subjects.

13. (Previously presented) A method of detecting a difference in expression of each of two or more genes of human test subjects vs. human control subjects;

a) using an oligonucleotide of predetermined sequence, detecting in RNA of a blood sample from said test subject which has not been fractionated into cell types, RNA encoded by said gene in said sample, wherein said gene is expressed in blood and in a non-blood tissue in a subject who is not said test subject, said oligonucleotide being specific only for RNA, or cDNA complementary to said RNA, encoded by said gene; and
b) quantifying a level of said amplification product; and
c) determining a difference between said level and a quantified level of control RNA encoded by said gene in RNA of blood samples which have not been fractionated into cell types from said one or more control subjects, said control RNA having been detected in said samples for said control subjects; wherein said difference for each said gene is indicative of diabetes in said test subject, thereby detecting a difference in expression of each said gene in said collection of two or more genes in blood of said human test subjects vs. said human control subjects.

14. (Previously presented) A method of detecting a difference in expression of a gene of a human test subject vs. human control subjects, said method comprising:

a) producing amplification products from RNA of a blood sample from said test subject which has not been fractionated into cell types, using primers specific only for RNA and/or cDNA complementary to said RNA, encoded by said gene, wherein said gene is expressed in blood and in a non-blood tissue of a subject who is not said test subject;
b) quantifying a level of said amplification product; and
c) determining a difference between said quantified level of said amplification

products and a quantified level of amplification products produced using primers specific only for RNA and/or cDNA complementary to said RNA, encoded by said gene, applied to control RNA of blood samples which have not been fractionated into cell types from said control subjects, wherein detection of said difference for said gene is indicative of diabetes in said test subject, thereby detecting a difference in expression of each said gene in said collection of two or more genes in blood of said human test subjects vs. said human control subjects.

15. (Previously presented) A method of detecting a difference in expression of each of two or more genes of a human test subject vs. human control subjects, said method comprising:

for each gene of said collection of two or more genes:

a) producing an amplification product from RNA of a blood sample from said test subject which has not been fractionated into cell types, using primers specific only for RNA and/or cDNA complementary to said RNA, encoded by said gene, wherein said gene is expressed in blood and in a non-blood tissue of a subject who is not said test subject; and and

b) quantifying a level of said amplification product,

c) determining a difference between said quantified level of said amplification product and a quantified level of amplification products produced using primers specific only for RNA and/or cDNA complementary to said RNA, encoded by said gene applied to control RNA of blood samples which have not been fractionated into cell types from said control subjects, said control RNA having been detected in said samples from said control subjects, wherein determining a difference for each said gene is indicative of diabetes in said test subject,

thereby detecting a difference in expression of each said gene in said collection of two or more genes in blood of said human test subjects vs. said human control subjects.

16. (canceled)

17.(Previously presented) The method of any one of claims 12-15, wherein each of said genes is selected from the genes listed in Table 3G.

18. (canceled)

19. (Currently amended) The method of any one of claims 12-15, wherein said diabetes is either symptomatic or asymptomatic.

20. (Previously presented) The method of any one of claims 12-15, wherein said diabetes is type II diabetes.

21.-24. (canceled)

25. (Previously presented)The method of any one of claims 1-4 and 12-15, further comprising the step of isolating RNA from said samples.

26. (Currently amended) The method of any one of claims 1-2 and 12-13, wherein said steps of determining said levels of RNA encoded by said gene in step (a) and/or step (b) is effected using quantitative RT-PCR (QRT-PCR).

27. (Canceled)

28. (Currently amended) The method of any one of claims 3-4 4-4 and 14-15 12-16, wherein said primers are 15-25 nucleotides in length.

29. (Canceled)

30. (Currently amended) The method of any one of claims 1-4 and 12-15 12-16, wherein the step of determining said levels of RNA encoded by each of said genes in step (a) and/or step (b) is by hybridizing a first plurality of isolated nucleic acid molecules that correspond to said genes to an array comprising a second plurality of isolated nucleic acid molecules.

31. (Original) The method of claim 30, wherein said first plurality of isolated nucleic acid molecules comprises RNA, DNA, cDNA, PCR products or ESTs.

32. (Original) The method of claim 30, wherein said array comprises a plurality of isolated nucleic acid molecules comprising RNA, DNA, cDNA, PCR products or ESTs.

33. (Canceled)

34. (Original) The method of claim 32, wherein said array comprises two or more of the markers of claim 2.

35. (Original) The method of claim 32, wherein said array comprises two or more of the markers of claim 3.

36. (Original) The method of claim 32, wherein said array comprises two or more of the markers of claim 4.
37. (Original) The method of claim 32, wherein said array comprises a plurality of nucleic acid molecules that correspond to genes of the human genome.
38. (Original) The method of claim 32, wherein said array comprises a plurality of nucleic acid molecules that correspond to two or more sequences of two or more genes selected from the group of genes listed in Table 3G.
39. (Original) A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 1.
40. (Original) A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 2.
41. (Original) A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 3.
42. (Original) A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 4.
- 43.(Canceled)
44. (Original) An array consisting essentially of the plurality of nucleic acid molecules of claim 39.
45. (Original) An array consisting essentially of the plurality of nucleic acid molecules of claim 40.
46. (Original) An array consisting essentially of the plurality of nucleic acid molecules of claim 41.
47. (Original) An array consisting essentially of the plurality of nucleic acid molecules of claim 42.
48. (Original) A kit for diagnosing or prognosing diabetes comprising:
 - a) two gene-specific priming means designed to produce double stranded DNA complementary to a gene that corresponds to a marker selected from the group consisting of markers of claim 1, claim 2, claim 3, and claim 4; wherein said first priming means

contains a sequence which can hybridize to RNA, cDNA or an EST complementary to said gene to create an extension product and said second priming means capable of hybridizing to said extension product;

- b) an enzyme with reverse transcriptase activity;
- c) an enzyme with thermostable DNA polymerase activity; and
- d) a labeling means;

wherein said primers are used to detect the quantitative expression levels of said gene in a test subject.

49. (Original) A kit for monitoring a course of therapeutic treatment of diabetes, comprising:

- a) two gene-specific priming means designed to produce double stranded DNA complementary to a gene that corresponds to a marker selected from the group consisting of markers of claim 1, claim 2, claim 3, and claim 4; wherein said first priming means contains a sequence which can hybridize to RNA, cDNA or an EST complementary to said gene to create an extension product and said second priming means capable of hybridizing to said extension product;
- b) an enzyme with reverse transcriptase activity;
- c) an enzyme with thermostable DNA polymerase activity; and
- d) a labeling means;

wherein said primers are used to detect the quantitative expression levels of said gene in a test subject.

50. (Original) A kit for monitoring progression or regression of diabetes, comprising:

- a) two gene-specific priming means designed to produce double stranded DNA complementary to a gene that corresponds to a marker selected from the group consisting of markers of claim 1, claim 2, claim 3, and claim 4; wherein said first priming means contains a sequence which can hybridize to RNA, cDNA or an EST complementary to said gene to create an extension product and said second priming means capable of hybridizing to said extension product;
- b) an enzyme with reverse transcriptase activity;
- c) an enzyme with thermostable DNA polymerase activity; and
- d) a labeling means;

wherein said primers are used to detect the quantitative expression levels of said gene in a test subject.

51. (Original) The kit of any one of claims 48 to 50 wherein said gene-specific priming means identified in step a) is selected from the group of genes listed in Table 3G.

52. (Original) A plurality of nucleic acid molecules that identify or correspond to two or more sequences of two or more genes selected from the group of genes listed in Table 3G.

53. (Canceled)

54. (Previously presented) The method of any of claims 1-4 wherein none of said control subjects have diabetes.

55. (Previously presented) The method of any of claims 1-4 wherein said control subjects have diabetes at a different stage than said subjects having diabetes.

56. (Previously presented) A method of identifying a marker useful for detecting diabetes, said method comprising:

a) using an oligonucleotide of predetermined sequence, detecting a presence in RNA of unfractionated cells of a lysed blood sample from subjects having diabetes, of RNA encoded by a gene, said gene expressed in blood and in a non-blood tissue of a subject not having diabetes, said oligonucleotide being specific only for RNA, or cDNA complementary to said RNA, encoded by said gene in said samples,

b) quantifying a level of said RNA encoded by said gene; and

c) determining a difference between said quantified level and a quantified level of a control RNA encoded by said gene in RNA of unfractionated cells of a lysed blood sample from control subjects, said control RNA having been detected in said samples from said control subjects,

thereby identifying said gene as being a marker useful for detecting diabetes.

57. (Previously presented) A method of identifying two or more markers useful for detecting diabetes, said method comprising:

for each of a collection of two or more genes

a) using an oligonucleotide of predetermined sequence, detecting a presence in RNA of

unfractionated cells of a lysed blood sample from subjects having diabetes of RNA encoded by said gene, said oligonucleotide being specific only for RNA, or cDNA complementary to said RNA, encoded by said gene in said samples, said gene being expressed in blood and in a non-blood tissue of a subject not having diabetes;

b) quantifying a level of said RNA encoded by said gene; and

c) determining a difference between said quantified level and a quantified level of control RNA encoded by said gene in RNA of unfractionated cells of a lysed blood sample from control subjects, said control RNA having been detected in said samples from said control subjects,

thereby identifying said two or more genes as two or more markers useful in detecting diabetes.

58. (Previously presented) A method of identifying a marker useful for detecting diabetes, said method comprising:

a) producing amplification products from RNA of unfractionated cells of a lysed blood sample, from subjects having diabetes, using primers specific only for RNA, and/or cDNA complementary to said RNA, encoded by a gene in said samples, said gene being expressed in blood and in a non-blood tissue of a subject not having diabetes;

b) quantifying a level of said amplification products; and

c) determining a difference between said quantified level of said amplification products and a quantified level of amplification products produced using primers specific only for RNA, and/or cDNA complementary to said RNA, encoded by said gene from control RNA, in RNA of unfractionated cells of a lysed blood sample, said control RNA having been detected in said samples from said control subjects,

thereby identifying said gene as being a marker useful for detecting diabetes.

59. (Previously presented) A method of identifying two or more markers useful for detecting diabetes said method comprising:

for each of a collection of two or more genes:

a) producing amplification products from RNA of unfractionated cells of a lysed blood sample from subjects having diabetes, using primers specific only for RNA, and/or

cDNA complementary to said RNA, encoded by said gene of said subjects, wherein said gene is expressed in blood and in a non-blood tissue of a subject not having diabetes;

b) quantifying a level of said amplification products; and

c) Determining a difference between said quantified level of said amplification products and a quantified level of amplification products produced using primers specific only for RNA, and/or cDNA complementary to said RNA, encoded by said gene, from control RNA in RNA of unfractionated cells of a lysed blood sample, from control subjects, said control RNA having been detected in said samples from said control subjects,

thereby identifying said collection of said two or more genes as two or more markers useful for detecting diabetes.

60. (Previously presented) A method of detecting a difference in expression of a gene in a human test subject as compared with human control subjects, said method comprising:

a) using an oligonucleotide of predetermined sequence, detecting in RNA of a unfractionated cells of a lysed blood sample of said test subject, RNA encoded by said gene in said sample, wherein said gene is expressed in blood and in a non-blood tissue in a subject who is not said test subject, said oligonucleotide being specific only for RNA or cDNA complementary to said RNA, encoded by said gene;

b) quantifying a level of said RNA encoded by said gene; and

c) determining a difference between said level and a quantified level of control RNA encoded by said gene in RNA of unfractionated cells of a lysed blood sample from said control subjects, wherein said difference is indicative of diabetes in said test subject,

thereby detecting a difference in expression of said gene in said human test subject vs. said human control subjects.

61. (Previously presented) A method of detecting a difference in expression of each of two or more genes of a human test subjects vs. human control subjects:

for each gene of a collection of said two or more genes:

a) using an oligonucleotide of predetermined sequence, detecting in RNA of a unfractionated cells of a lysed blood sample from said test subject, RNA encoded by said

gene in said sample, wherein said gene is expressed in blood and in a non-blood tissue in a subject who is not said test subject, said oligonucleotide being specific only for RNA, or cDNA complementary to said RNA, encoded by said gene;

b) quantifying a level of said RNA encoded by said gene; and

c) determining a difference between said level and a quantified level of control RNA encoded by said gene in RNA of unfractionated cells of a lysed blood sample from said control subjects, said control RNA having been detected in said samples for said control subjects; wherein said difference for each said gene is indicative of diabetes in said test subject,

thereby detecting a difference in expression of each said gene in said collection of two or more genes in blood of said human test subjects vs. said human control subjects.

62. (Previously presented) A method of detecting a difference in expression of a gene of a human test subject vs. human control subjects, said method comprising:

a) producing amplification products from RNA of a blood sample unfractionated cells of a lysed blood sample from said test subject, using primers specific only for RNA and/or cDNA complementary to said RNA, encoded by said gene, wherein said gene is expressed in blood and in a non-blood tissue of a subject who is not said test subject;

b) quantifying a level of said amplification product; and

c) determining a difference between said quantified level of said amplification products and a quantified level of amplification products produced using primers specific only for RNA and/or cDNA complementary to said RNA, encoded by said gene, applied to control RNA of unfractionated cells of a lysed blood sample from said control subjects, wherein detection of said difference for said gene is indicative of diabetes in said test subject,

thereby detecting a difference in expression of said gene in blood of said human test subject vs. human control subjects.

63. (Previously presented) A method of detecting a difference in expression of each of two or more genes of a human test subject vs. human control subjects, said method comprising: for each gene of said collection of two or more genes:

a) producing an amplification product from RNA of a unfractionated cells of a lysed blood sample from said test subject, using primers specific only for RNA and/or cDNA complementary to said RNA, encoded by said gene, wherein said gene is expressed in blood and in a non-blood tissue of a subject who is not said test subject; and

b) quantifying a level of said amplification product,

c) determining a difference between said quantified level of said amplification product and a quantified level of amplification products produced using primers specific only for RNA and/or cDNA complementary to said RNA, encoded by said gene applied to control RNA of unfractionated cells of a lysed blood sample from said control subjects, said control RNA having been detected in said samples from said control subjects, wherein detecting a difference for each said gene is indicative of diabetes in said test subject,

thereby detecting a difference in expression of each said gene in said collection of two or more genes in blood of said human test subjects vs. said human control subjects.

64. (Previously presented) A method for detecting diabetes in a human test subject, comprising:

- a) Quantifying in RNA of a blood sample from said test subject, a level of RNA encoded by the gene DAZ interacting protein 1 (DZIP1) in said sample; and
 - b) Comparing said quantified level with a quantified level of control RNA encoded by said gene in RNA of blood samples from control subjects;
- wherein said comparison of said quantified level of step (a) with said quantified level of said control RNA is indicative of diabetes in said human test subject.
65. (Previously presented) The method of claim 64, wherein said blood sample of step (a) and said blood samples from said control subjects in step (b) have not been fractionated into cell types.
66. (Previously presented) The method of claim 64, wherein said blood sample of step (a) and said blood samples from said control subjects in step (b) are unfractionated samples of lysed blood.

67. (Previously presented) The method of any of claims 64, 65 and 66, wherein said quantifying of said level of said RNA encoded by said gene in step (a) is effected by quantifying said RNA relative to a housekeeping gene.
68. (Previously presented) The method of any of claims 64, 65 and 66, wherein said quantifying of said level of said RNA encoded by said gene in step (a) is effected by quantification of cDNA corresponding to said RNA.
69. (Previously presented) The method of any of claims 64, 65 and 66, wherein said control subjects do not have diabetes and said comparison of step (b) results in a statistically significant difference.
70. (Previously presented) The method of any of claims 64, 65 and 66, wherein said control subjects have been diagnosed as having diabetes and said comparison results in a statistically significant similarity.
71. (Previously presented) The method of any of claims 64, 65 and 66, wherein said quantifying of said level of said RNA encoded by said gene in step (a) is determined using quantitative real-time RT-PCR.
72. (Previously presented) The method of any of claims 64, 65 and 66, wherein said quantifying of said level of said RNA encoded by said gene in step (a) is determined using an array.